

**Amendment and Response**

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Serial No.: 09/738,599

Confirmation No.: 1240

Filed: 15 December 2000

For: NUCLEIC ACID ENCODING AN AVIAN *E. COLI* ISS POLYPEPTIDE AND METHODS OF USE**Remarks**

The Office Action mailed 30 July 2004 has been received and reviewed. Claims 31, 32, 37, 45, 67, 68, and 70 having been amended, and claim 43 having been cancelled, the pending claims are claims 30-33 and 35-70. Reconsideration and withdrawal of the rejections are respectfully requested.

**The 35 U.S.C. §112, First Paragraph, Rejection**

Claims 43 and 70 and claims 45 and 67 dependent therefrom are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner alleged that there was no descriptive support for an 'immunogenic subunit' or 'immunogenic fragment' of the nucleic acid molecule in the instant specification, as originally filed. Therefore, the Examiner alleged that the limitations in the claims are considered to be new matter.

Claim 43 has been cancelled, thereby rendering the rejection of claim 43 moot. In view of the cancellation of claim 43, claim 44 has been amended to depend upon claim 45.

Claim 70 has been amended to remove the second recitation of "or an immunogenic subunit or immunogenic fragment thereof."

Reconsideration and withdrawal of the present rejection is respectfully requested.

**The 35 U.S.C. §112, Second Paragraph, Rejection**

Claims 31, 32, 37-45, 67, and 70 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

As noted above, claim 43 has been cancelled, and claim 70 has been amended to remove the second recitation of "or an immunogenic subunit or immunogenic fragment thereof."

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The phrase "an immunogenic fragment or immunogenic subunit" was considered unclear in whether the phrase referred to the claimed nucleic acid molecule or the polypeptide encoded by the nucleic acid molecule. A person of ordinary skill would recognize that this phrase defines the metes and bounds of the claims. Even if this phrase caused the metes and bounds of the claims to not be readily recognizable to one of skill in the art, the meaning of the term is clear in view of the disclosure. In the interests of furthering prosecution, claims 37 and 68 have been amended to recite "an immunogenic fragment or immunogenic subunit of the polypeptide."

Claims 31, 32, and 45 are amended to insert the indefinite article "the" before the word nucleotides.

Reconsideration and withdrawal of the present rejection is respectfully requested.

**The 35 U.S.C. §102 Rejection**

Claims 37-40, 43, 67, and 68 are rejected under 35 U.S.C. §102(b) as being anticipated by Barondess et al., "A Bacterial Virulence Determinant Encoded by Lysogenic Coliphage  $\lambda$ ," *Nature*, 346(6287):871-874 (1990) as evidenced by Harlow et al., in "Antibodies: A laboratory Manual," Cold Spring Harbor Laboratory, Chapter 5, page 76 (1988). This rejection is respectfully traversed.

"During examination, the claims must be interpreted as broadly as their terms reasonably allow (citations omitted). This means that the words of the claim must be given their plain meaning unless applicant has provided a clear definition in the specification (citations omitted). . . . It is only when the specification provides definitions for terms appearing in the claims that the specification can be used in interpreting claim language (citations omitted)." M.P.E.P. § 2111.01.

Independent claims 37 and 68 each recite an "immunogenic composition." The specification defines "immunogenic composition" as referring "to a composition or preparation administered in an amount effective to raise antibodies in a recipient and *further provides some therapeutic benefit or effect so as to result in an immune response that inhibits or prevents a septicemic disease in a subject*, or so as to result in the production of antibodies to a virulent

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complement resistant avian *E. coli* isolate, or polypeptide or peptide employed as an immunogen." Specification at page 43, lines 19-24, emphasis added. Thus, independent claims 37 and 68 are directed to compositions that, inter alia, provide "some therapeutic benefit or effect so as to result in an immune response that inhibits or prevents a septicemic disease in a subject."

In the Examiner's view, "Barondess' PBS-suspended bacterial host cells comprising the above-identified nucleotide sequence inherently serve as immunogenic compositions." Action, page 5. Applicants disagree.

The Examiner has not provided any evidence as to why the nucleotide sequence cited in the Action inherently serves as an immunogenic composition. Specifically, the Examiner provides no evidence that the nucleotide sequence cited in the Action encodes a polypeptide that *provides some therapeutic benefit or effect so as to result in an immune response that inhibits or prevents a septicemic disease in a subject*, in order to support reliance on a theory of inherency under 35 U.S.C. §102(b).

"In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art" (emphasis in original). M.P.E.P §2112. "The fact that a certain result or characteristic may occur or be present in the prior art is not sufficient to establish the inherency of that result or characteristic" (emphasis in original). M.P.E.P §2112. "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing may result from a given set of circumstances is not sufficient.' " M.P.E.P §2112. Applicants maintain that the doctrine of inherency is not available to supplement the demonstrated deficiencies of the cited documents, because the Examiner has not provided any evidence that the nucleotide sequence cited in the Action encodes a polypeptide that provides some therapeutic benefit or

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effect so as to result in an immune response that inhibits or prevents a septicemic disease in a subject.

For this reason alone the cited document does not anticipate claims 37-40, 43, 67, and 68.

Furthermore, the Examiner states that "Barondess' PBS-suspended bacterial host cells comprising the above-identified nucleotide sequence inherently serve as immunogenic compositions" and the "cells expressing the polypeptide are contained in PBS (i.e., a pharmaceutically acceptable carrier)." Action at page 5. This is irrelevant, as independent claims recite an immunogenic composition comprising "an *isolated* nucleic acid molecule . . . and a pharmaceutically acceptable carrier."

The Examiner also states that the "products are contained in PBS, i.e., a pharmaceutically acceptable carrier (see page 873)." Action at page 5. The only reference to PBS that appears to be made at page 873 of Barondess et al. is at Table 1, and this refers to cells, not an *isolated* nucleic acid molecule as recited in independent claims 37 and 68.

For at least these reasons, reconsideration and withdrawal of the rejection of claims 37-40, 43, 67, and 68 as anticipated under the cited art is respectfully requested.

**The 35 U.S.C. §103 Rejection**

Claims 37 and 41 are rejected under 35 U.S.C. §103(a) as being unpatentable over Barondess et al., "A Bacterial Virulence Determinant Encoded by Lysogenic Coliphage  $\lambda$ ," *Nature*, 346(6287):871-874 (1990) in view of our submission of the art in an Information Disclosure Statement. This rejection is respectfully traversed.

The burden is on the Examiner to establish a *prima facie* case of obviousness of the claimed invention, and it is respectfully argued that the Examiner has fallen far short of meeting this burden. The three criteria that must be met (MPEP § 2143) are:

- (i) there must be a suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings;
- (ii) there must be a reasonable expectation of success; and

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(iii) the prior art reference (or references when combined) must teach or suggest all the claim limitations.

It is respectfully submitted that the Examiner is failed to establish the presence of any suggestion or motivation to modify the cited art.

The M.P.E.P. notes that "[i]n determining the propriety of the Patent Office case for obviousness in the first instance, it is necessary to ascertain whether or not the reference teachings would appear to be sufficient for one of ordinary skill in the relevant art having the reference before him to make the proposed substitution, combination, or other modification." M.P.E.P. §2143.01. The M.P.E.P. elaborates further on this concept by requiring that "the references must expressly or impliedly suggest the claimed invention or the examiner must present a convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious in light of the teachings of the references." MPEP §706.02(j). Moreover, "[t]he mere fact that references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination." MPEP §2143.01 (emphasis added).

The Examiner asserts that "[o]ne of skill in the art would have been motivated to produce the instant invention for the expected benefit of improved expression of Barondess' polynucleotide since improved expression is ideally desired in the art." Action at page 6. It is respectfully submitted that a skilled person desiring improved expression of a nucleotide sequence normally expressed in *E. coli* would *not* be motivated to express the nucleotide sequence in an animal cell. At the time the present application was filed microbial cells, especially *E. coli*, were regarded as more desirable for protein expression than animal cells. For instance, microbial cells were known in the art as growing much faster than animal cells, requiring a much less complex and less expensive growth medium, and expressing higher levels of protein. If the skilled person were seeking improved expression of a nucleotide sequence normally expressed in *E. coli*, why would they express the sequence in animal cells? The Examiner has not provided a convincing line of reasoning as to why the artisan would have found the claimed invention to have been obvious.

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The Examiner is requested to note that the present specification suggests that the skilled person could use animal cells for the expression of polypeptides; however, it does not state that the skilled person would be motivated to use an animal cell for expression of polypeptides. In this regard, the Examiner is requested to note that a "statement that modifications of the prior art to meet the claimed invention would have been 'well within the ordinary skill of the art at the time the claimed invention was made' because the references relied upon teach that all aspects of the claimed invention were individually known in the art is *not sufficient* to establish a prima facie case of obviousness without some objective reason to combine the teachings of the references." M.P.E.P. §2143.01 (emphasis added). The Examiner may have provided an objective reason, i.e., improved expression, but the skilled person that seeks improved expression of a bacteriophage gene would not be motivated to use animal cells.

"The tendency to resort to 'hindsight' based upon applicant's disclosure is often difficult to avoid due to the very nature of the examination process. However, impermissible hindsight must be avoided and the legal conclusion must be reached on the basis of the facts gleaned from the prior art." M.P.E.P. § 2142. The Examiner has not provided any reason why the skilled person would use an animal cell for improved expression of a bacteriophage gene, and has merely taken the applicant's disclosure and used it as a blueprint for putting together a rejection to defeat the patentability of the present invention.

For at least these reasons, reconsideration and withdrawal of the rejection of claims 37 and 41 as obvious in view of the cited art is respectfully requested.

Claim 42 is rejected under 35 U.S.C. §103(a) as being unpatentable over Barondess et al., "A Bacterial Virulence Determinant Encoded by Lysogenic Coliphage  $\lambda$ ," *Nature*, 346(6287):871-874 (1990) and Krieg et al. (WO 96/02555). This rejection is respectfully traversed.

It is respectfully submitted that there is no motivation to combine Barondess et al. and Krieg et al. to arrive at the present invention. The Office asserts that "[o]ne of skill in the art would have been motivated to produce the instant invention for the expected benefit of further enhancing the immune response to Barondess' (1990) product" (Action, page 7).

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The statement made by the Office at page 7 of Action may show that the documents could be combined to have the Barondess et al. product together with Krieg's immunostimulatory sequence; however, it does not provide any convincing line of reasoning as to why a skilled person would combine the documents. For instance, no convincing line of reasoning is provided regarding why the skilled person would want to have an immune response to the Barondess et al. product.

It is respectfully submitted that this rejection is another example of the use of hindsight by the Examiner. The cited documents, viewed by themselves and not in retrospect, must suggest doing what applicant has done. In re Shaffer 108 USPQ 326, 329 (CCPA 1956). The cited documents do not suggest doing what the applicants have done.

For at least these reasons, the Office is respectfully requested to reconsider and withdraw the rejection of 42 under 35 U.S.C. §103(a) as being unpatentable over Barondess et al., "A Bacterial Virulence Determinant Encoded by Lysogenic Coliphage  $\lambda$ ," *Nature*, 346(6287):871-874 (1990) and Krieg et al. (WO 96/02555).

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It is respectfully submitted that the pending claims 30-33, 37-45, and 67-70 are in condition for allowance and notification to that effect is respectfully requested. The Examiner is invited to contact Applicants' Representatives, at the below-listed telephone number, if it is believed that prosecution of this application may be assisted thereby.

Respectfully submitted for  
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**CERTIFICATE UNDER 37 CFR §1.8:**

The undersigned hereby certifies that the Transmittal Letter and the paper(s), as described hereinabove, are being transmitted by facsimile in accordance with 37 CFR §1.6(d) to the Patent and Trademark Office, addressed to Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 1<sup>st</sup> day of November, 2004, at 2:48 p.m. (Central Time).

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